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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BADIO, BARBARA P	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/776,757	PAIRET ET AL.	
	Examiner	Art Unit	
	Barbara P. Badio	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,9,10,15-17,19-21,23,25,26,31-37,39 and 63-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,9,10,15-17,19-21,23,25,26,31-37,39 and 63-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Office Action on the Merits

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Application

2. Claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 are pending in the present application.

Claim Rejections - 35 USC § 112

3. The rejection of claims 5-8, 18, 22, 27-20 and 38 under 35 USC 112, first paragraph, scope of enablement is made moot by the cancellation of the instant claims.

4. The rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 under 35 USC 112, first paragraph, scope of enablement is maintained.

Applicant argues (a) the claims are limited to specific compounds, i.e., tiotropium and ciclesonide; (b) adequate enablement is inclusive of what is known by those of ordinary skill in the art; (c) the question should be "can one of ordinary skill in the art conduct routine experimentation to provide the solvates and hydrates of the claimed compounds which would be useful for carrying out the invention and can one of ordinary skill in the art routinely determine the nature of any such solvates or hydrates"; and (d)

only routine experimentation is needed to make solvates or hydrates. Applicant's argument was considered but not persuasive for the following reasons.

The claimed invention as amended is a composition comprising (i) a tiotropium salt and (ii) ciclesonide in the form of "their enantiomers, mixtures of their enantiomers, their racemates, their solvates or their hydrates".

The issue is whether the present specification and the knowledge in the art at the time of the present invention provide adequate enablement for the recitation of "solvates and/or hydrates" of tiotropium and ciclesonide.

According to applicant, the question is not whether "it is routine or predictable to determine whether a specific solvent or water will form a solvate or hydrate with a specific compounds and the nature of such solvate or hydrate" but whether "one of ordinary skill in the art can conduct routine experimentation to provide the solvates and hydrates of the claimed compounds which would be useful for carrying out the invention and can one of ordinary skill in the art routinely determine the nature of any such solvates or hydrates". The examiner notes that the right question was asked, i.e., whether the formation of solvates or hydrate of a compound is routine or predictable.

Based on the knowledge in the art as evidenced by the references provided in the previous Office Action, the formation of solvates or hydrates is neither routine nor predictable. That is, the skilled artisan might be able to conduct experimentation to provide solvates and hydrates of a compound however, said experimentation is not routine or predictable especially since one can not predict (a) whether a compound

might form solvates or hydrates and (b) a particular solvent would form a solvate with a particular compound.

Lastly, the present specification lacks the guidance necessary to make solvates or hydrates of the claimed compounds as well as examples of said solvates or hydrates of tiotropium and ciclesonide. Because of the lack of teaching in the present specification and the unpredictability in the art as it relates to the formation of solvates and hydrates, the skilled artisan would have to engage in undue experimentation to determine solvents that would form solvates and hydrates of the claimed compounds.

For these reasons and those given in the previous Office Action, the rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 under 35 USC 112, first paragraph, scope of enablement is maintained.

Double Patenting

5. The provisional rejection of claim 1 on the ground of nonstatutory obviousness-type double patenting over claims of copending Applications 11/006/940; 11/068,134; 11/109,094; 11/169,876, 11/267,354; 10/392,558 and 10/735,959 is withdrawn.

6. The provisional rejection of claim 1 on the ground of nonstatutory obviousness-type double patenting over claims of copending Application 11/424,244 is maintained.

Applicant argues none of the claims in the copending application is directed to "such a specific combination of components". Applicant's argument was considered but not persuasive for the following reasons.

The cited copending application is inclusive of "pharmaceutical compositions" comprising a tiotropium salt and teaches the addition of additional active ingredients to the composition such as ciclesonide (see page 58, line 16 of the cited copending application). '244 also teaches inhalable powder pharmaceutical compositions comprising sugars such as glucose, arabinose, lactose, saccharose and maltose (see page 21, line 33 – page 22, line 9 of the cited copending application). Therefore, the production of a pharmaceutical composition as claimed by '244, including those of the instant claims, would be prima facie obvious.

For these reasons and those given in the previous Office Action, the provisional rejection of claim 1 on the ground of nonstatutory obviousness-type double patenting over claims of copending Application 11/424,244 is maintained.

Claim Rejections - 35 USC § 103

7. The rejection of claims 5-8, 18, 22, 27-30 and 38 under 35 USC 103 over Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is made moot by the cancellation of the instant claims.

8. The rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 under 35 USC 103 over Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

Applicant argues the combination of references provides no suggestion of the claimed composition and Banholzer provides no teachings of any steroid. Applicant also argues the references do not provide any teaching regarding the particular excipients and that the claimed composition shows unexpected advantages. Applicant's argument was considered but not persuasive for the following reasons.

(a) Nishimura is directed to the use of corticosteroids in combination of oxitropium bromide, an anticholinergic agent in the treatment of chronic asthma. The reference exemplifies beclomethasone diproprionate as the corticosteroid. However, (a) Nishimura is evaluated for what it teaches and not just what is exemplified and (b) ciclesonide is a well known corticosteroid. Therefore, the use of any corticosteroid in combination with an anticholinergic agent, such as oxitropium bromide, would be obvious to the skilled artisan in the art.

(b) Banholzer teaches esters of thienyl carboxylic acids and amino alcohols such as tiotropium are strong anticholinergic agents with prolonged action useful in treating asthma. Banholzer also teaches the compounds are therapeutically stronger than ipratropium bromide, another known anticholinergic agent.

(c) Sugars such as those recited by the instant claims are known excipients for preparation of inhalable powder (see for example, US 6,645,466, col. 8, lines 1-16).

As shown above, each of tiotropium, an anticholinergic agent and ciclesonide, a corticosteroid is useful in treating asthma. The claimed combination is prima facie based on the recognized utility as discussed above and the utilization of combination therapy in the medical/pharmaceutical art. The addition of known carriers to an otherwise obvious composition does not lend patentability to said composition.

Applicant argues unexpected advantages. As noted by applicant said data is not in declaration form. Additionally, the examiner notes that applicant does not make comparison of the claimed composition with any combination of a corticosteroid and an anticholinergic agent. Although the prior art does not exemplify the combination of a tiotropium salt and ciclesonide, it does exemplify the combination of a corticosteroid and an anticholinergic agent and the beneficial effect of said combination. Banholzer provides motivation to utilize an ester of thienyl carboxylic acids and amino alcohols such as tiotropium, as the anticholinergic agent based on the teaching of prolonged action and therapeutically stronger property.

For these reasons and those given in the previous Office Action, the rejection of claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 under 35 USC 103 over Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination is maintained.

9. Claims 1, 3, 4, 9, 10, 15-17, 19-21, 23, 25, 26, 31-37, 39 and 63-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keller et al. (WO 00/28979, see

English equivalent US 6,645,466), Nishimura et al. (Allergology International, 1999) and Banholzer et al. (US 5,610,163) in combination.

Keller et al. teaches dry powder formulations for inhalation (see the entire article, especially claims 1-11; Example 6). Keller also teaches (a) preferred dry powder formulations containing a β-mimetic and/or an anticholinergic and/or a corticosteroid (see for example, col. 6, line 52 – col. 7, line 10); (b) the use of known carriers for the preparation of dry powder formulations such as glucose, lactose, sucrose, etc. (see col. 8, lines 1-16); (c) anticholinergics such as tiotropium bromide and corticosteroids such as ciclesonide (see col. 6, line 52 – col. 7, line 11) and (d) carrier particle size of approximately 10 to 500 μg (see col. 7, lines 40-53).

Nishimura et al. teaches an inhalation composition comprising anticholinergic agents, such as, oxitropium bromide and ipratropium bromide and corticosteroids such as beclomethasone dipropionate for treating asthma (see the entire article, especially page 85, col. 2, Introduction; page 87, Table 1 and Discussion). Nishimura teaches the addition of oxitropium bromide to corticosteroids such as beclomethasone dipropionate shows beneficial effects (see page 87, col. 1, Discussion, 1st paragraph).

Banholzer et al. teaches esters of thienyl carboxylic acids and amino alcohols such as tiotropium and its salts as strong anticholinergic agents for use in treating asthma (see the entire article, especially col. 3, line 23 - col. 4, line 9; col. 5, compound A). Banholzer also teaches the compounds show similar toxicity to ipratropium bromide while at the same time the therapeutic effect is stronger (see col. 3, lines 27-32).

Based on the combination of the above cited references, the preparation of a dry powder inhalation formulation comprising an anticholinergic agent, such as a tiotropium salt and a corticosteroid, such as ciclesonide would have been obvious to the skilled artisan in the art at the time of the present invention. The motivation to combine an anticholinergic agent with a corticosteroid is based on (a) the knowledge in the art of the utilization of each in treating similar conditions such as asthma and (b) the teaching by Nishimura of the beneficial effect of said combination. The motivation to utilize tiotropium as the anticholinergic agent is based on the teaching of Banholzer of the increase therapeutic effect and prolonged action of esters of thienyl carboxylic acids and amino alcohols.

The recitation of (a) weight ratios of anticholinergic to steroid (see claims 9 and 10); (b) capsule containing the claimed composition (see claims 25, 26, 31-37) and (c) a kit containing the claimed composition (see claims 63-66) are noted.

Banholzer teaches various formulations including capsules (see '163, col. 4, lines 3-9) and, thus, the recitation of capsules containing the claimed composition is prima facie obvious. Additionally, weight ratio of the active ingredients and kits are not patentable over the prior art as discussed above because (a) the court has held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233 and (b) incorporation of known agents into kits are well known in the medical art. Therefore, the instantly claimed invention would have been obvious to one of skilled in the art at the time of the present invention.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Telephone Inquiry

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara P. Badio/
Primary Examiner, Art Unit 1612